Durvalumab with platinum-based chemotherapy, then with or without olaparib, for treating newly diagnosed advanced or recurrent endometrial cancer [ID6317]

Technology appraisal committee A [6 May 2025]

PART 1
For screen – confidential information redacted

Chair: James Fotheringham

External assessment group: BMJ

Technical team: Tom Palmer, Jo Richardson, Emily Crowe

Company: AstraZeneca

Durvalumab with platinum-based chemotherapy, then with or without olaparib, for treating newly diagnosed advanced or recurrent endometrial cancer [ID6317]

- ✓ **Background and recap of committee conclusions from ACM1**
- ❑ Consultation responses

NICE National Institute for Health and Care Excellence

Durvalumab (Imfinzi®) and olaparib (Lynparza®) (AstraZeneca)

Marketing authorisations Granted December 2024	**Durvalumab** • Durvalumab with carboplatin and paclitaxel is indicated for 1st line treatment of adults with primary advanced or recurrent endometrial cancer who are candidates for systemic therapy, followed by maintenance treatment with: ↳ Durvalumab monotherapy in mismatch repair deficient (dMMR) endometrial cancer ↳ Durvalumab with olaparib in mismatch repair proficient (pMMR) endometrial cancer **Olaparib** Maintenance treatment of adults with primary advanced or recurrent pMMR endometrial cancer whose disease has not progressed on 1st line durvalumab with carboplatin and paclitaxel.
Administration	**Durvalumab:** • Induction: 1,120 mg intravenously with carboplatin + paclitaxel every 21 days for 4 to 6 cycles • Maintenance: 1,500 mg every 4 weeks **Olaparib:** 300 mg orally twice daily (600 mg daily dose)
Duration	'Until disease progression or unacceptable toxicity'
Price	Confidential commercial access agreements in place for durvalumab and olaparib

NICE dMMR, mismatch repair deficient; pMMR, mismatch repair proficient.

Draft recommendation at ACM1

dMMR – recommended

- Durvalumab with platinum-based chemotherapy, then maintenance durvalumab monotherapy, can be used as an option for untreated primary advanced or recurrent endometrial cancer that is mismatch repair deficient (dMMR) in adults who can have systemic treatment.
- Should be stopped after 3 years, or earlier if disease progression or unacceptable toxicity.

Note stopping rule is **not** in marketing authorisation or used in DUO-E trial. Informed by clinical advice

pMMR – not recommended

Durvalumab with platinum-based chemotherapy, then maintenance durvalumab plus olaparib, should not be used for untreated primary advanced or recurrent endometrial cancer that is mismatch repair proficient (pMMR) in adults who can have systemic treatment.

Requested analysis:

- ↳ p53 mutated subgroup within pMMR population – clinical experts noted this is area of unmet need that may get greater benefit from durvalumab plus olaparib

Uncertainties	• Long-term benefit • Generalisability of subsequent treatment use in DUO-E • Implementation of stopping rule
Acceptable ICER	around £20,000 per QALY
Decision	• dMMR**:** committee's preferred ICER within cost-effectiveness range • pMMR: company and EAG base cases and committee's preferred ICER substantially above the range to be considered cost effective

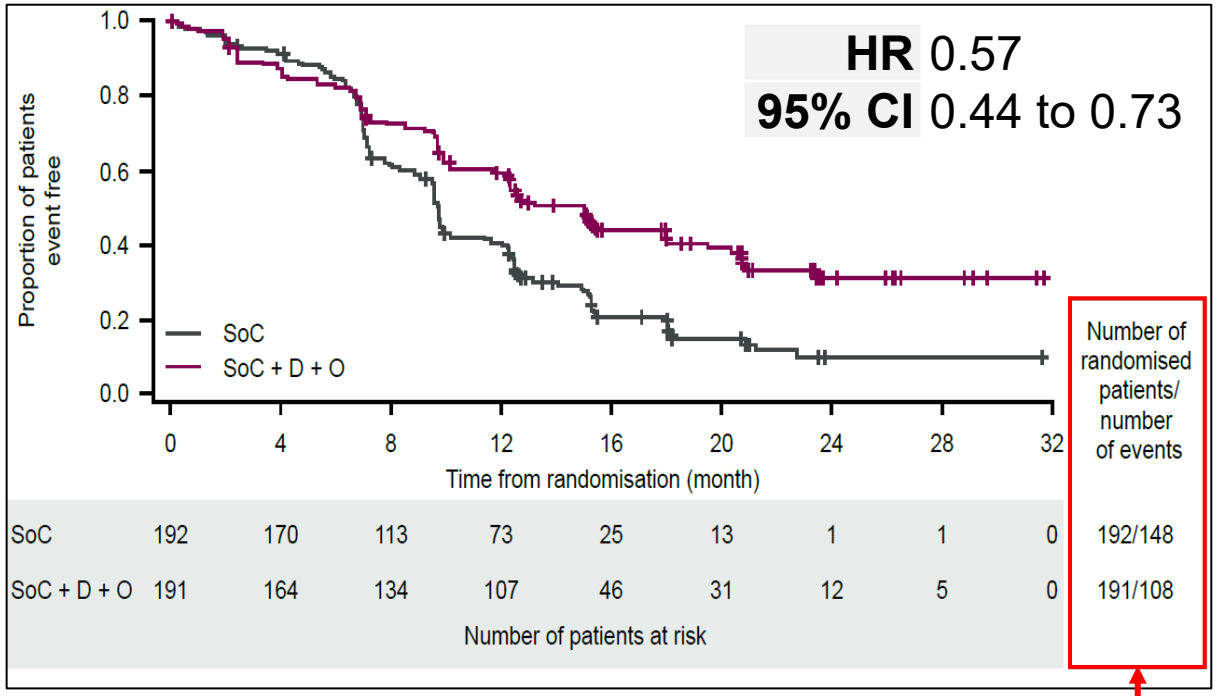
dMMR, mismatch repair deficient; ICER, incremental cost-effectiveness threshold; pMMR, mismatch repair proficient; QALY, quality-adjusted life year.

DUO-E – pMMR PFS and OS

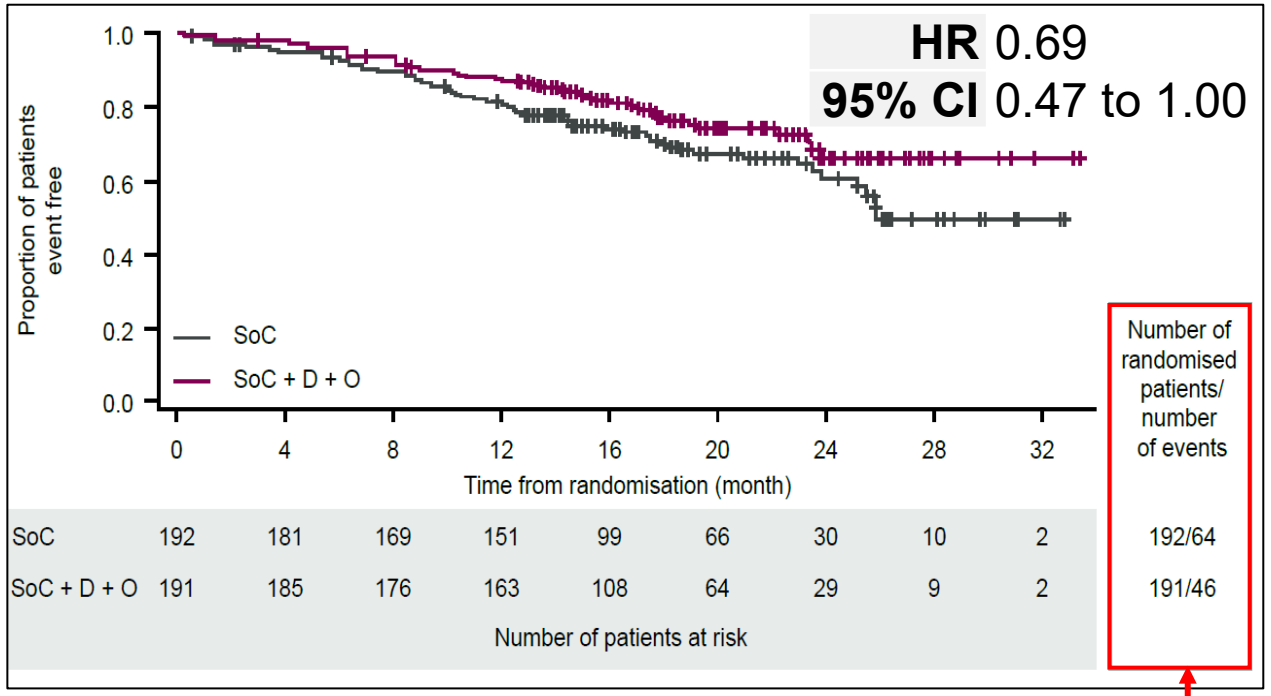
Durvalumab improves PFS vs. SoC, but HR for OS includes 1

See appendix for PFS and OS extrapolations

PFS (investigator-assessed)
SoC (n=192) compared with SoC+D+O (n=191)



OS
SoC (n=192) compared with SoC+D+O (n=191)



EAG: Immaturity of data makes extrapolations (particularly for OS) highly uncertain – further data needed

NICE CI, confidence interval; HR, hazard ratio; MA, marketing authorisation; OS, overall survival; PFS, progression-free survival; pMMR, mismatch repair proficient; SoC+D+O, standard of care plus durvalumab plus olaparib.

pMMR base case differences and committee preference

Assumption	Company base case	EAG base case
Treatment duration cap	3 years	None
TTD extrapolation	Log-logistic with 3-year treatment cap	Exponential
Proportion of patients initiating olaparib (pMMR)	[redacted] (Of all patients in SoC+D+O arm, proportion who had olaparib maintenance in DUO-E)	[redacted] (Of all patients who had any maintenance treatment in SoC+D+O arm, proportion who had olaparib maintenance in DUO-E)
Drug wastage	Excluded	Included
Subsequent treatment administration cost	SB15Z from NHS reference costs 2021/22 (£399.92)	SB15Z – from NHS reference costs 2022/23 (£393.16)

[redacted] = Committee preference

See appendix for dMMR base cases

dMMR, mismatch repair deficient; pMMR, mismatch repair proficient; SoC+D+O, standard of care plus durvalumab plus olaparib; TTD, time to treatment discontinuation.

Durvalumab with platinum-based chemotherapy, then with or without olaparib, for treating newly diagnosed advanced or recurrent endometrial cancer [ID6317]

- ❑ Background and recap of committee conclusions from ACM1
- ✓ **Consultation responses**

NICE National Institute for Health and Care Excellence

Summary of consultation responses received

AstraZeneca (company)

- Welcomes recommendation of SoC+D for dMMR endometrial cancer
- Willing to accept committee's preferred assumptions for pMMR, but:
  - Challenges the chosen £20,000 per QALY threshold for pMMR
  - Considers uncertainty has been overestimated by committee and disagrees that uncertainties stated should lead to lowest bound of NICE's usual willingness-to-pay threshold range
  - Thinks threshold should be higher given unmet need, potential to address health inequalities, and limited uncertainties
  - Note DUO-E trial provides compelling evidence for SoC+D+O for all people with pMMR endometrial cancer, regardless of p53 status. Therefore no rationale to consider p53 subgroup analyses.

NHS England Cancer Drugs Fund lead

- Noted that the proportion initiating olaparib maintenance assumption may be incorrect

Peaches Womb Cancer Trust

- Highlighted potential equality issues from negative pMMR draft recommendation

Clinical expert

- 'Further follow-up may show better evidence for pMMR population, but think only a subset will get enough benefit to warrant cost'

dMMR, mismatch repair deficient; pMMR, mismatch repair proficient; QALY, quality-adjusted life year; SoC+D, standard of care plus durvalumab; SoC+D+O, standard of care plus durvalumab plus olaparib.

Olaparib maintenance initiation

ACM1 committee considerations

- Olaparib costs applied in the model to a proportion of people alive and progression-free after week 18
- Committee preferred (+ company base case): [redacted]% (% of all patients in SoC+D+O arm who had olaparib)
- EAG base case: [redacted]% (% of patients who had any maintenance treatment who had olaparib)
- Clinical experts: EAG base case too high – company more plausible. Likely somewhere between

NHSE Cancer Drugs Fund lead

- For pMMR, intent at outset of treatment must be to use both D+O as maintenance treatment
- Patients must start both D+O at maintenance, and cannot have only one as monotherapy
- Dose reductions/delays expected for some patients
- D or O can be stopped independently of the other due to, for example, unacceptable toxicity
- If patients have a true contraindication to starting either, then they are disqualified from use of D+O for pMMR

In DUO-E:

- [redacted] patients with pMMR assigned SoC+D+O
  - [redacted] initiated olaparib maintenance
  - [redacted] did not initiate olaparib maintenance
    a. [redacted] had disease progression
    b. [redacted] continued durvalumab monotherapy
    c. [redacted] were ineligible, such as not meeting maintenance eligibility criteria, discontinuation due to adverse events, patient choice
    d. [redacted] patients unaccounted for

What proportion should be assumed to initiate olaparib maintenance?

NICE D, durvalumab; O, olaparib; pMMR, mismatch repair proficient; SoC+D+O, standard of care plus durvalumab plus olaparib.

Equality concerns

ACM1 committee considerations

- '…incidence rates and mortality for endometrial cancer are higher in the Black ethnic group…'
- 'Black ethnic groups may also have more aggressive histology and may be more likely to have molecular subtypes with a poorer prognosis.'
- 'The committee considered whether [the negative recommendation] could indirectly discriminate against people in Black ethnic groups'
- 'The committee considered that [any indirect discrimination] would be a proportionate means of achieving the legitimate aim of maximising public health… as SoC+D+O was not cost-effective for pMMR'

Peaches Womb Cancer Trust consultation response

- Inequality in access to new treatments for people with pMMR endometrial cancer, especially at 1st line
  - ↳ Leaves patients frustrated, abandoned and hopeless
- Racial disparities in pMMR molecular profiles, aggressive p53abn subtype over-represented in Black women
- Black ethnic groups more likely to have late diagnosis and have higher risk of death

Company consultation response

- Restricting durvalumab will worsen racial and socioeconomic inequalities in treatment of endometrial cancer

Has the committee seen anything to change its conclusions on equality from ACM1?

NICE

pMMR, mismatch repair proficient; SoC+D+O, standard of care plus durvalumab plus olaparib.

Uncertainty (1) – long-term benefit

See appendix for DUO-E immaturity, and PFS and OS extrapolations

ACM1 committee considerations

- DUO-E trial data were immature at primary cut off – 66.1% PFS events, 29.2% OS events
- 'The committee concluded that the short follow up and immaturity of the DUO-E results means that the clinical-effectiveness data is uncertain'

Company consultation response

- Almost all oncology appraisals have limited follow-up and some inherent uncertainty
- OS extrapolations validated by clinicians + the EAG considered them reasonable
- Scenario analyses showed that plausible alternative OS extrapolations reduced the ICER
- Highlight that dostarlimab 1st line dMMR appraisal (TA963) had similar uncertainty around long-term outcomes, but £25,000 per QALY threshold was applied

EAG comments

- Dostarlimab appraisal (TA963) in a different population (dMMR) so cannot be directly compared to pMMR
- Clinical advice: 'dMMR endometrial cancer tends to respond better to immunotherapy, while pMMR endometrial cancer is very heterogeneous'

Do concerns about uncertainty in long-term benefit remain?

dMMR, mismatch repair deficient; ICER, incremental cost-effectiveness threshold; OS, overall survival; PFS, progression-free survival; QALY, quality-adjusted life year.

Uncertainty (2) – subsequent treatments in DUO-E

See appendix for ACM1 slide

ACM1 committee considerations

- Issue 1: 2nd line immunotherapy use in SoC arm was lower than expected in NHS
- Issue 2: 2nd line immunotherapy use in SoC+D+O arm was allowed in DUO-E ([redacted] had it), but is not in NHS
- 'The committee concluded that the differences in subsequent immunotherapy use between DUO-E and NHS practice was an unresolvable uncertainty'

Company consultation response

- Issue 1 only applies to dMMR – in pMMR, 2nd line immunotherapy use in SoC arm is generalisable to NHS ([redacted]% in DUO-E vs. [redacted]% expected from clinical advice)
- Issue 2 – company accept that 2nd line immunotherapy use for SoC+D+O arm not reflective of NHS, but:
  - ↳ No evidence that immunotherapy rechallenge is an effective strategy
  - Patients rechallenged in DUO-E least likely to get benefit, if any exists, as they had progression while on 1st line immunotherapy. Clinicians and evidence from other cancers suggest that most likely patients to benefit from rechallenge are those who have progression after treatment-free interval

EAG comments

- Delinking of trial results with model outcomes – subsequent treatments removed from SoC+D+O costs, but any benefits were captured in OS extrapolations – may [redacted] costs and [redacted] efficacy

Do concerns about uncertainty with subsequent treatments remain?

Uncertainty (3) – implementation of stopping rule

See appendix for ACM1 slides

ACM1 committee considerations

- License permits treatment to progression, but company model 3-year stopping rule
- DUO-E did not contain a similar stopping rule, but has not yet released data from longer than 3 years
- Clinical experts confirmed that NHS uses immunotherapies to progression or stops at 2 or 3 years
- 'The committee concluded that despite some uncertainty, the 3-year treatment duration cap in the company's model is appropriate for decision making'

Company consultation response

- Evidence shows immunotherapy treatment benefit typically appears in 2 to 3 years
- As clinical experts confirmed – treatment would stop at 3 years in NHS
- Implementation of stopping rule is therefore not an uncertainty – aligns model treatment duration to NHS practice

EAG comments

- Again, separates trial results from modelled outcomes
- Adds certainty to the modelled costs incurred in the NHS, but adds uncertainty in the modelled outcomes – NHS PFS and OS likely to differ from trial due to stopping rule, but unknown to what extent

Do concerns about uncertainty with the stopping rule remain?

OS, overall survival; PFS, progression-free survival

Uncaptured benefits

ACM1 committee considerations

- Considered durvalumab with platinum-based chemotherapy, then with or without olaparib, could be an innovative treatment
- No routinely available 1st line immunotherapies for endometrial cancer
- High unmet need in pMMR particularly
- 'Committee agreed to take these additional benefits into account in its decision making.'

Company consultation response

- People with pMMR cancer can only access immunotherapy at 2nd line, after their cancer has progressed and/or their health has worsened
- Lack of effective 1st line treatment has a negative psychological impact on patients

Has the committee seen anything to change its conclusions on uncaptured benefits?

NICE pMMR, mismatch repair proficient.

Summary of key questions for committee

	Question for committee
ACM1 conclusions	Has the committee seen anything to change its assessment of the: 1. Equality concerns? 2. Uncertainties? a. Long-term benefit b. Generalisability of subsequent treatment use in DUO-E c. Implementation of stopping rule d. Proportion initiating olaparib maintenance treatment 3. Uncaptured benefits?
ICER threshold	Accounting for the consultation responses on equalities, uncertainties, and uncaptured benefits, what is the committee's preferred cost-effectiveness threshold?

 ICER, incremental cost-effectiveness ratio.

Cost-effectiveness results

All ICERs are reported in PART 2 slides

because they include confidential discounts

pMMR subgroup

- Company and EAG base case ICERs are both substantially above £30,000 per QALY gained
- Committee preferred ICER is substantially above £30,000 per QALY gained

Supplementary appendix

NICE National Institute for Health and Care Excellence

Background on endometrial cancer

Primary advanced or recurrent endometrial cancer has a poor prognosis

Diagnosis and classification

- Primary advanced endometrial cancer (stages 3 and 4) is cancer which started in the uterus but has spread to other parts of the body. Approx 20% of cases diagnosed at this stage.
- Mismatch repair helps cells to correct mutations in DNA which can cause cancer – endometrial cancer can be mismatch repair deficient (dMMR) or proficient (pMMR)
- dMMR tumours are more likely to have high levels of mutation, and typically respond better to immunotherapy

Symptoms and prognosis

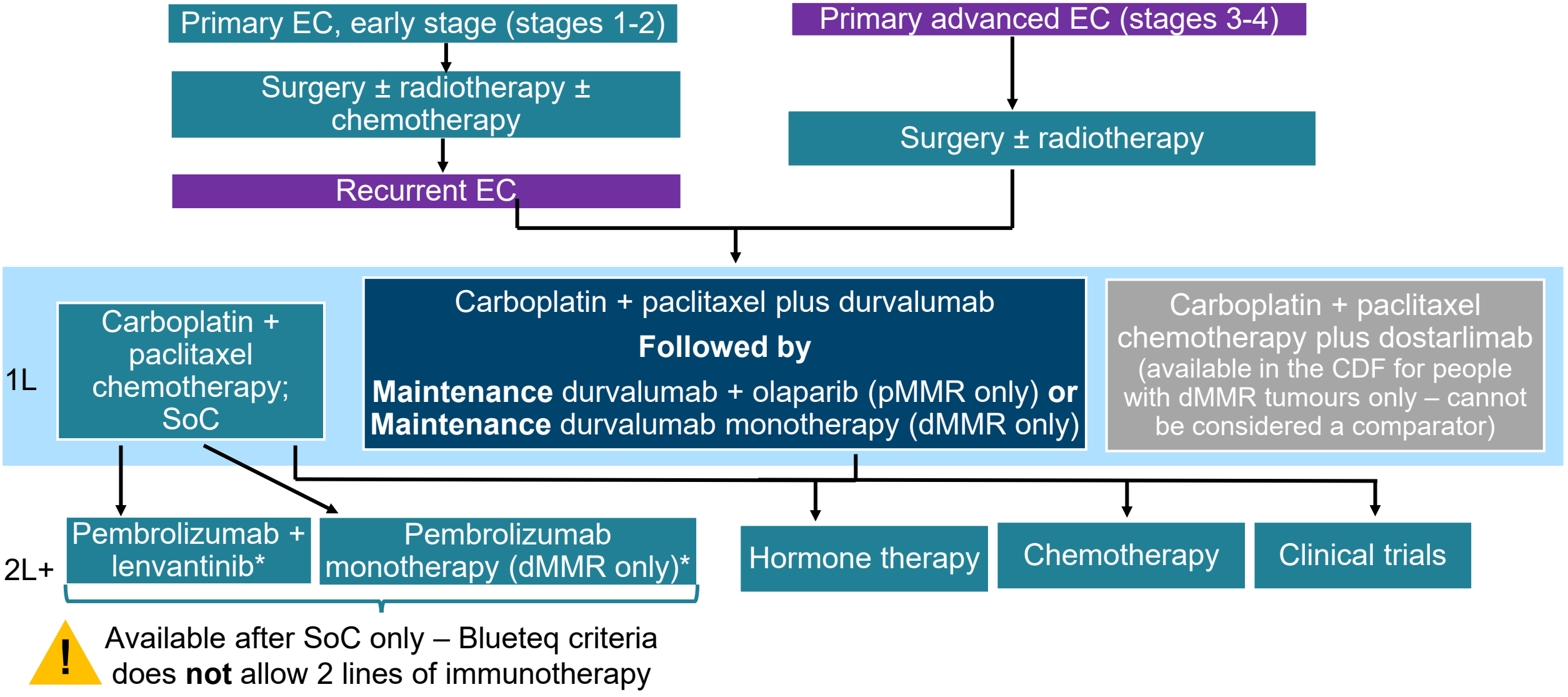
- Unusual vaginal bleeding, pelvic pain, lump in abdomen or pelvis, unintended weight loss
- 5-year survival rate is 48% for stage 3 cancer, 15% for stage 4, 20% for recurrent disease

dMMR, mismatch repair deficient; pMMR, mismatch repair proficient.

Treatment pathway

= Intervention

EAG – treatment pathway in line with current clinical practice



! Available after SoC only – Blueteq criteria does **not** allow 2 lines of immunotherapy

CDF, Cancer Drugs Fund; dMMR, mismatch repair deficient; EC, endometrial cancer; pMMR, mismatch repair proficient; SoC, standard of care.

Key clinical trial – DUO-E

Design	Phase 3 randomised, double-blind, placebo-controlled trial
Population	Adults (n=718) with newly diagnosed advanced (stage 3 or 4) EC or recurrent epithelial EC with low cure potential from surgery (excluding sarcomas)
Interventions	• Durvalumab with carboplatin + paclitaxel, maintenance durvalumab + placebo (SoC+D) (n=238, n=46 dMMR) • Durvalumab with carboplatin + paclitaxel, maintenance durvalumab + olaparib (SoC+D+O) (n=239, n=191 pMMR)
Comparator	Carboplatin + paclitaxel + placebo, placebo maintenance (SoC) (n=192 pMMR, n=49 dMMR)
Follow-up	Median follow up SoC: 12.6 months Median follow up SoC+D+O and SoC+D: 15.4 months
Key outcomes	PFS (primary), OS, ORR, DoR, TTD, QoL
Locations	Global across 22 countries (no UK patients)
Key subgroups	Mismatch repair status (dMMR or pMMR) – pre-specified for PFS only

EAG: Randomisation stratified by MMR status, but trial did not exclusively randomise dMMR patients to receive SoC+D or pMMR patients to receive SoC+D+O to match marketing authorisation

dMMR, mismatch repair deficient; DoR, duration of response; EC; endometrial cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; pMMR, mismatch repair proficient; QoL, quality of life; SoC, standard of care; SoC+D, standard of care plus durvalumab; SoC+D+O, standard of care plus durvalumab plus olaparib; TTD, time to treatment discontinuation.

Back to main deck

Key issue: Immaturity of DUO-E data

EAG – outcome data is very immature (particularly for OS) – uncertainty is significant

Maturity of outcomes as of primary DCO (April 2023):

Outcomes	Maturity (n/N) - dMMR subgroup		Maturity (n/N) - pMMR subgroup	
	SoC	SoC+D	SoC	SoC+D+O
PFS	51.0% (25/49)	32.6% (15/46)	77.1% (148/192)	56.5% (108/191)
OS	36.7% (18/49)	15.2% (7/46)	33.3% (64/192)	24.1% (46/191)
TTD	-	[redacted]	-	[redacted]

Company

- Validated long term survival using committee discussion from appraisal of dostarlimab in dMMR endometrial cancer (TA963)
- Further analysis expected in Q4 2025 (expected 87% of target OS events), final DCO predicted for 2026

EAG

- Immaturity of data makes extrapolations (particularly for OS) highly uncertain – further data needed
- Company's use of TA963 for validation problematic as committee considered there was uncertainty in these clinical results (and the preferred approach for OS was undecided)

DCO; data cut off; dMMR, mismatch repair deficient; OS, overall survival; PFS, progression-free survival; pMMR, mismatch repair proficient; SoC, standard of care; SoC+D, standard of care plus durvalumab; SoC+D+O, standard of care plus durvalumab plus olaparib; TTD, time to treatment discontinuation.

Subsequent treatment usage

Back to main deck

Background

- In DUO-E, [redacted]% of dMMR patients on SoC+D and [redacted]% of pMMR patients on SoC+D+O receiving subsequent treatments had immunotherapies - but 2nd immunotherapy use not part of UK practice
- Subsequent immunotherapy use in SoC arms [redacted] than expected in UK practice [redacted]

Company

- Re-challenge with immunotherapy not permitted in UK clinical practice according to Blueteq criteria
- Dostarlimab excluded from dMMR subsequent treatments in SoC arm of model (only in CDF) - proportions updated to assume increased usage of pembrolizumab monotherapy (in line with clinical expert opinion)

EAG comments

- Clinical efficacy may be [redacted]
- EAG's clinical experts [redacted]
- Company's adjustment of subsequent treatment proportions to capture costs of SoC without dostarlimab is reasonable, but no real-world data to validate this

How does the difference in subsequent immunotherapy use in UK practice affect the generalisability of the data?

NICE

CDF, Cancer Drugs Fund; dMMR, mismatch repair deficient; OS, overall survival; pMMR, mismatch repair proficient; SoC, standard of care; SoC+D. standard of care plus durvalumab; SoC+D+O; standard of care plus durvalumab plus olaparib.

Back to main deck

PFS extrapolations for pMMR subgroup

For both SoC and SoC+D+O, EAG considers company's log-logistic extrapolation appropriate

PFS KM curves, and log-logistic extrapolations for SoC and SoC+D+O in the PMMR subgroup:

Year	SoC (%)		SoC+D+O (%)	
	KM	Log-logistic	KM	Log-logistic
1	[redacted]	[redacted]	[redacted]	[redacted]
2	[redacted]	[redacted]	[redacted]	[redacted]
3	-	[redacted]	-	[redacted]
5	-	[redacted]	-	[redacted]
10	-	[redacted]	-	[redacted]

EAG

- Company explored flexible spline models – but analysis demonstrated these did not offer meaningful advantages over standard parametric models
- Changes in chosen PFS extrapolation are not a key driver of cost effectiveness

NICE

KM, Kaplan-Meier; OS, overall survival; pMMR, mismatch repair proficient; SoC, standard of care; SoC+D, standard of care plus durvalumab.

Back to main deck

OS extrapolations for pMMR subgroup

EAG – company's extrapolations reasonable but more mature OS data still needed

OS KM curves, lognormal extrapolations and log-logistic extrapolations for SoC and SoC+D+O:

[redacted]

Year	SoC (%)		SoC+D+O (%)	
	KM	Log-logistic	KM	Log-logistic
1	[redacted]	[redacted]	[redacted]	[redacted]
2	[redacted]	[redacted]	[redacted]	[redacted]
3	-	[redacted]	-	[redacted]
5	-	[redacted]	-	[redacted]
10	-	[redacted]	-	[redacted]

EAG

- Company has validated OS estimates for SoC against published data and long-term OS estimates not unreasonable. If using the same type of distribution for treatment arms of a model, then not unreasonable to apply to SoC+D+O in absence of more long-term data
- Significant uncertainty in OS data due to immaturity – benefits of subsequent immunotherapy may not be fully captured in extrapolations

KM, Kaplan-Meier; OS, overall survival; pMMR, mismatch repair proficient; SoC, standard of care; SoC+D, standard care plus durvalumab.

dMMR base case differences and committee preference

Assumption	Company base case	EAG base case
Survival extrapolation for PFS in SoC + D	2-knot spline	1 knot spline
OS distribution	Log-normal	Log-logistic
Treatment duration cap	3 years	None
TTD extrapolation	Gamma with 3-year treatment cap	Gamma
Drug wastage	Excluded	Included
Subsequent treatment administration cost	SB15Z from NHS reference costs 2021/22 (£399.92)	SB15Z – from NHS reference costs 2022/23 (£393.16)

= Committee preference

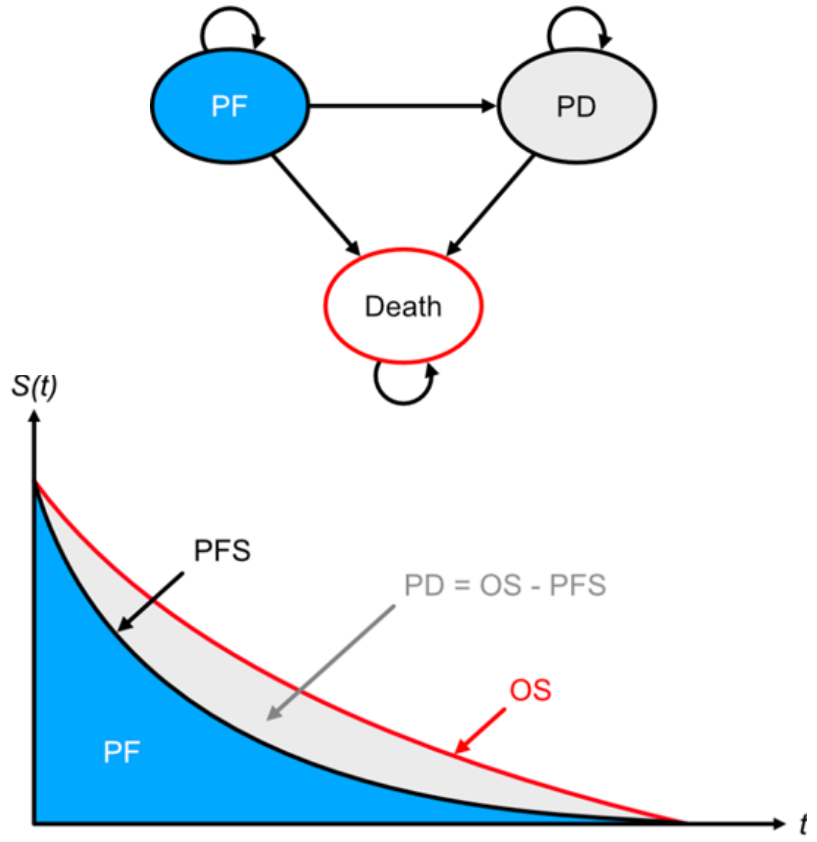
Back to main deck

dMMR, mismatch repair deficient; OS, overall survival; PFS, progression-free survival; SoC+D, standard of care plus durvalumab; TTD, time to treatment discontinuation

Company's model overview

Three state partitioned survival model with dMMR and pMMR modelled separately

Model structure



- Technology affects **costs** by:
  - Increasing drug acquisition costs
- Technology affects **QALYs** by:
  - Increasing survival
- Assumptions with greatest ICER effect:
  - Method for estimating long-term survival for dMMR patients
  - Duration of treatment with durvalumab and olaparib
  - Proportion of progression-free pMMR patients starting maintenance treatment with olaparib in addition to durvalumab.

EAG: Model structure is appropriate

dMMR, mismatch repair deficient; ICER, incremental cost-effectiveness ratio; OS, overall survival; PFS, progression-free survival; pMMR, mismatch repair proficient; QALY, quality-adjusted life year; TTD, time to treatment discontinuation.

How company incorporated evidence into model for its original base case

Input	Assumption and evidence source
Baseline characteristics	Based on final analysis (FAS) of ITT population (mean age 62.6 years)
Intervention and comparator efficacy	DUO-E individual patient level data (split by MMR subgroup)
Time horizon	Lifetime (38 years)
Utilities	EQ-5D-5L data from patients in DUO-E, mapped to EQ-5D-3L
Cycle length	1 month (PFS and OS), 1 week (TTD)
Discount rate	3.5%
Costs	BNF, NHS NCC, PSSRU and eMIT
Resource use	Routine costs informed by TA963 and DUO-E resource use data. One off terminal care cost applied (sourced from PSSRU)
Subsequent treatment	Based on DUO-E trial data and UK clinical expert opinion, [redacted] of progressed patients have subsequent treatment (regardless of MMR status)
Treatment waning	None

BNF; British National Formulary; eMIT, electronic market information tool; ITT; intention to treat; MMR, mismatch repair; NCC, National Cost Collection; OS, overall survival; PFS, progression-free survival; PSSRU, Personal Social Services Research Unit; TTD; time to treatment discontinuation.

Back to main deck

Cap on treatment duration

Background

- Company model assumes treatment with olaparib and durvalumab continues until disease progression or up to a maximum treatment duration of 3 years
  - DUO-E treatment regimen – continue until disease progression or unacceptable toxicity

Company

- Assumption of treatment duration cap aligns with other EC immunotherapies
- Discontinuation prior to progression or toxicity may occur in clinical practice
  - Company clinical experts – patients expected to discontinue immunotherapy within five years (due to remission), with discussions at 1-3 years depending on response

EAG comments

- Cap on treatment duration artificially limits intervention acquisition costs
- Uncertainty in long-term efficacy estimates with a hard cap on treatment duration due to immaturity of data
- Company has not explored treatment waning assumptions after artificial treatment duration cap
- SPC says treatment should continue until disease progression or unacceptable toxicity – EAG prefers no cap on treatment duration with TTD extrapolations tending to 0:
  - dMMR = gamma distribution preferred (in line with company approach to TTD)
  - pMMR = exponential distribution preferred

- Should there be a cap on treatment duration in the model?
- If yes, does committee need to consider a stopping rule?
- If no cap is preferred, what is the appropriate extrapolation of TTD in pMMR and dMMR?

dMMR, mismatch repair deficient; EC, endometrial cancer; pMMR, mismatch repair proficient; SPC, summary of product characteristics; TTD; time to treatment discontinuation

Back to main deck

Cap on treatment duration

Stopping rules in other immunotherapies for EC:

Immunotherapy	Stopping rule in SPC	Stopping rule in clinical trials	Additional stopping rule in NICE recommendation
Dostarlimab (TA779*, TA963*) (dMMR/high MSI EC only)	Until disease progression or unacceptable toxicity, or for a duration of up to 3 years	GARNET (key trial for TA779) - none RUBY (key trial for TA963) – 3 years	N/A – stopping rule in SPC
Pembrolizumab monotherapy (TA914)	None for EC	KEYNOTE-158 (key trial for EC in TA914) - 2 years	2 years of uninterrupted treatment, or earlier if the cancer progresses
Pembrolizumab with lenvatinib (TA904)	None for EC	KEYNOTE-775 - 2 years for pembrolizumab, lenvatinib until clinical progression	None

* Recommendations in CDF only

- Should there be a cap on treatment duration in the model?
- If yes, does committee need to consider a stopping rule?
- If no cap is preferred, what is the appropriate extrapolation of TTD in pMMR and dMMR?

dMMR, mismatch repair deficient; EC, endometrial cancer; pMMR, mismatch repair proficient; SPC, summary of product characteristics; TTD; time to treatment discontinuation